# DRAFT

**Written Testimony Pertaining to *The Green Chemistry Research and Development Act of 2004***

**Berkeley W, Cue, Jr.**
**Pfizer, Inc**

**(First slide showing)**

Good morning Chairman Boehlert and members of the House Science Committee. I want to take this opportunity to thank you for the invitation to be here today to describe Pfizer's efforts around green chemistry and to help you understand why we believe green chemistry is a critical ingredient in our company's approach to corporate citizenship and in developing more efficient research processes.

Over the next few minutes I will do my best to address three topics. First, I will describe Pfizer's green chemistry activities and, in doing so, indicate how we believe these investments are paying off. Also, I will state as clearly as I can what we believe are the environmental and human health benefits of pursuing green chemistry.

I will address some important impediments to pursuing green chemistry solutions and provide some context to help the members of this committee understand which areas could possibly benefit from more federal involvement in green chemistry

Finally, I will share with you my views on *The Green Chemistry Research and Development Act of 2004.*

**Slide 2**

First, let me begin by telling you about Pfizer. Pfizer was founded in 1849 in Brooklyn New York. The majority of the penicillin that went ashore with the Allied forces on D-day was made by Pfizer using a novel deep vat fermentation process. Today, we are the world's leading healthcare company, with more than 130,000 employees worldwide, over $45 billion in annual sales reported for 2003, more drugs rated number one in their therapeutic class in sales volume than any other company, we have over 200 potential products in our R&D pipeline and we spent over $7 Billion in 2003 to discover, develop, register, and commercialize these products. In addition to prescription human health care we have a large consumer health, or over-the counter drug business and are ranked first in animal healthcare as well. I work in Pfizer Global R&D in the Groton, Connecticut Laboratories. There I lead the departments that are responsible for the design and optimization of the manufacturing processes for our active drug (API) and dosage forms such as tablets, capsules, and injectable formulations. I also lead the company's green chemistry efforts, working with colleagues around the world.

## Slide 3

When a company achieves this sustained level of success we are expected to provide leadership. Pfizer is committed to a business model that is sustainable. Our environmental, health and safety or EH&S policy is based on the International Chamber of Commerce Charter on Sustainable Development. The Brundtland Commission's report in "Our Common Future" in 1987 states that sustainable development meets the economic, environmental and social needs of the present without compromising the ability of future generations to meet their own needs.

In 2002 Pfizer was the first pharmaceutical company to sign the UN Global Compact, committing us to nine principles on human rights, labor and environmental performance.

Our purpose statement is to dedicate ourselves to humanity's quest for healthier, happier lives through innovation and our mission is to become the world's most valued company to patients, customers, colleagues, investors, business partners and the communities where we live and work. Green Chemistry helps make all of this achievable.

## Slide 4

So what is Green Chemistry? The best articulation I've found is the one proposed by Paul Anastas from the White House Office of Science and Technology Policy (OSTP) and John Warner, Director of the Center for Green Chemistry at the University of Massachusetts-Boston and a Pfizer consultant for green chemistry. "Green Chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products."

## Slide 5

### The Twelve Principles of Green Chemistry

1. **Prevention:** It is better to prevent waste than to treat or clean up waste after it has formed.
2. **Atom economy**: Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. **Less Hazardous Chemical Synthesis:** Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. **Design Safer Chemicals:** Chemical products should be designed to preserve efficacy of function while reducing toxicity.

5. **Safety Solvents and Auxiliaries:** The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and, innocuous when used.
6. **Design for Energy Efficiency**: Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.
7. **Use Renewable Feedstocks**: A raw material of feedstock should be renewable rather than depleting wherever technically and economically practicable.
8. **Reduce Derivatives**: Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided wherever possible.
9. **Catalysis:** Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. **Design for Degradation:** Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products. For the Pharmaceutical Industry this principle is especially challenging since we are required to demonstrate our drug to be stable in the dosage form for the shelf life of the product.
11. **Real-Time Analysis for Pollution Prevention** Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12. **Inherently Safer Chemistry for Accident Prevention**: Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions, and fires.

**Slide 6**

Now I will address some of the benefits we have achieved by practicing green chemistry. The general perception among chemists who are not savvy about green chemistry is that the environmental gain usually comes at an economic cost. In this slide we demonstrate that for every principle there is both an environmental and an economic benefit. Thus, green chemistry supports our corporate citizenship to both environmental and economic performance. Without a doubt, it has been a win-win proposition for Pfizer.

Pfizer has been practicing the principles of process development and optimization for a long time. When we became aware of green chemistry in the late 1990's it seemed to us that this approach offered several benefits. We found a strong level of alignment between our traditional approach to chemical synthesis and process optimization with many of the principles, as well as a new way of thinking about chemical at all scales-from milligram quantities in the laboratory to tens of thousands of kilograms produced commercially.

An analysis of the performance of the pharmaceutical industry in terms of process efficiency published by Roger Sheldon in 1994 determined that for every kilogram of drug produces between 25 and 100 kilograms of waste are produced. For those processes where we have applied green chemistry principles we have been able to reduce this number to between 5-10 kilos of waste per kilo of product. **A 5 to 10-fold improvement!** At commercial product volumes this equates to hundreds of thousands of kilos of waste prevented each year for each product where we have succeeded in finding a greener chemistry alternative. There is a double economic benefit here-we are not purchasing raw materials that are lost to unwanted byproducts and we do not incur the expense costs associated with treating and disposing of this waste.

There may be some who believe zero waste is achievable. My view is that in preparation of complex organic molecules the production of by products is unavoidable. The goal of our chemists is to make this number as small as is technically feasible.

**Slide 7**

In 2002 Pfizer was awarded a US EPA Presidential Green Chemistry Challenge Award for our improvements in the manufacturing process of sertraline hydrochloride, the active ingredient in our anti depression product Zoloft. Please note in the lower left corner of the slide, the substantial reduction in overall solvent usage as well as the complete elimination of the use of methylene chloride, a highly hazardous substance.

Green Chemistry objectives were emphasized in the redesign of the sertraline process, resulting in quality chemical transformations with dramatic environmental and worker safety improvements. Manufacturing yield has essentially doubled. The benign solvent ethanol, obtainable from biomass, is now used for three synthetic conversions. The hazardous dehydrating reagent titanium tetrachloride was eliminated. A more selective catalyst now drives more complete conversion of the starting materials to racemic sertraline. *In-situ* resolution of the diastereomeric salts, through highly selective crystallization, is now used to produce pure S,S-sertraline. Overall, two intermediate isolations and a salt conversion step were eliminated.

The environmental and safety improvements are dramatic. Use of approximately 140 metric tons/year of titanium tetrachloride and the generation of 440 metric tons/year of

problematic solid titanium dioxide wastes were eliminated. Approximately 150 metric tons/year of 35% HCl were eliminated. Neutralization of the highly acidic step 2, requiring approximately 100 metric tons/year of 50% NaOH, was eliminated. Consequently, high-salt waste streams are no longer produced. Dehydration additives and aqueous washes were eliminated, and the number and volume of solvents used were dramatically reduced. The efficiency of raw material, water, and energy use were dramatically improved.

The EPA is to be commended for sponsoring this award, not because we received it in 2002, but because it is contributing to raising the visibility of green chemistry and contributing to a cleaner, safer environment.

**Slide 8**

This slide demonstrates that, following green chemistry principles, similar dramatic improvements have been achieved for the manufacture of sildenafil citrate, the active ingredient in Viagra, our drug for treating erectile dysfunction. This improvement was recognized with a 2003 Crystal Faraday Award, presented by the Institute of Chemical Engineering in the United Kingdom. The efficiency factor for this process is below 10, down from a typical 25 or greater for pharmaceutical manufacturing processes developed in the absence of green chemistry considerations.

This year we have submitted three applications for US EPA Presidential Green Chemistry Challenge Awards for improvements in the manufacturing processes to celecoxib, the active ingredient in our anti arthritis agent Celebrex, for quinapril hydrochloride, the API in Accupril for treating high blood pressure and for sildenafil citrate, which I already described. Going forward all, major drug product manufacturing processes are being evaluated for green chemistry improvement potential. Like any R&D activity, not all efforts will be successful, but when we are the economic and environmental savings can be dramatic.

There are other benefits as well. Our leadership in green chemistry has improved our ability to attract and retain the best synthetic chemists in the marketplace. Today's graduating students are more environmentally conscious. They asked tough questions and we have good answers. Our green chemistry program allows us to communicate with external stakeholders about our commitment to corporate citizenship and sustainability. Last year we maintained our position in the pharmaceutical sector Dow Jones Sustainability Index, which enhances our shareholder value, in part because of our leadership in green chemistry.

**Slide 9**

Let me now address the question of impediments-focusing on three that are important to our industry.

1. **Academic training**: Today, there are very few students graduating with chemistry majors who are trained in or even exposed to green chemistry. In the slide shown now we are investing a huge amount of energy to educate our scientists about the green chemistry principles and how they apply to our daily R&D efforts. We would be in a much better place if the chemists who joined our company were practicing green chemistry on the first day of work. In addition to active education we sponsor R&D site based awards to encourage green chemistry. In addition to a trophy and public recognition the recipients are awarded a cash prize, with the stipulation that they donate it to a college or university of their choice to encourage green chemistry education. The legislation you are considering today should help support more focus on green chemistry education at the college and university levels. There are a few schools that do this very well today: U. Mass-Boston, Carnegie Mellon, University of Alabama, Washington State University, to mention some of them. More are needed.

**Slide 10**

To address this issue Pfizer has begun a program of reaching out to universities near our R&D sites to host symposia where students are exposed to green chemistry in real life case studies. They leave with a better understanding of how chemistry is practiced in the pharmaceutical industry and how green chemistry contributes to R&D success.

Another potential barrier to companies in our industry pursuing green chemistry solutions is the need to pay strict attention to the purity profile of the drugs we produce. By definition, an active pharmaceutical ingredient (API) is the active chemical and its normal process related substances (PRS's). This profile is established as part of the R&D process and is "qualified" as part of our preclinical animal safety studies and human clinical development experience. This profile is described in our regulatory submissions (New Drug Application in the US) and establishes the ranges for our product quality specifications. Changes in the manufacturing processes can create new process –related substances, easily detectable using modern analytical tools. Presence of these new PRS's at higher than allowed levels could necessitate redoing significant portions of development work, a time-consuming expensive and risky proposition. Every company has instances where processes which produce higher yields of cleaner product with a much better environmental profile, but were not pursued further because of this barrier. Obviously, using green chemistry earlier will lessen, but not remove this risk. In this case the goal of the FDA and the EPA may not always be mutually compatible. It is very important that we retain the flexibility to make business decisions that weigh and balance business risks with potential benefits.

One issue that has repeatedly surfaced in green chemistry discussions is whether consumers will pay for environmentally benign products. The consensus is that they will not.

Executive Order 13101 was signed in September 1998. In section 102, it states, "consistent with policies established by the Office of Federal Procurement Policy (OFPP)

agencies will comply with executive branch policies for the acquisition and use of environmentally preferable products and services and implement cost-effective procurement preference programs favoring the purchase of these products and services. We believe that companies that produce products derived from manufacturing processes consistent with green chemistry principles should qualify for consideration under this Executive Order.

As to the question of this specific legislation our experience teaches that an integrated approach to green chemistry at Pfizer that coordinates the efforts of R&D, Manufacturing and EH&S is a more effective way to create an effective green chemistry strategy. Prior to this we had a series of unconnected tactics, with no guarantee that we were gaining maximum benefit or that we were not seeing unnecessary duplication of effort.

The proposed legislation establishes a Green Chemistry R&D Program to promote and coordinate Federal green chemistry research, development, demonstration, education, technology transfer and commercial application activities. These are all critical components of Pfizer's successful green chemistry initiative. The availability of merit-reviewed competitive grants to support academic programs and to promote education and training of undergraduate and graduate students in green chemistry should help address the issue of lack of adequate green chemistry programs in academic institutions. The charge to the Federal Government to create incentives for use of green chemistry products and processes should help to address the issue I raised with respect to Executive Order 13101. Of specific interest to the Pharmaceutical industry would be the working relationship between this inter-agency group and reviewing chemists at the Food and Drug Administration. We believe that the levels of appropriation are appropriate for the initiation and sustaining of this program over the 2005-2007 timeframe.

**Slide 11**

In closing I would like to thank the committee for your attention. Green chemistry has the potential to produce the greatest change in the way synthetic chemistry is practiced in the last quarter century. It is already redefining how chemistry is thought about and practiced at every stage of R&D and commercial manufacture at Pfizer.

My crystal ball is no better at discerning the future than anyone's, but my prediction is that at some time in the future a Nobel Prize in Chemistry will be awarded to a green chemist. Our CEO, Dr. Hank McKinnell is fond of telling Pfizer employees, "the patient is waiting." In this context, it is clear that our environment is waiting too.

Thank you again for the opportunity to appear before you today and discuss Pfizer's Green Chemistry initiatives and the proposed legislation.